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LLNL BSL-3 EA - Assessment of the impact of recent NRC recommendations regarding the USAMRIID EIS

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Date: September 27, 2010

To: Thomas F. Gioconda, Deputy Director

From: George W Anderson, Jr., Select Agent Manager

Subject: *LLNL BSL-3 EA – Assessment of the impact of recent NRC recommendations regarding the USAMRIID EIS"*

Recent comments by the National Research Council (NRC) regarding the Environmental Impact Statement (EIS) for another federal laboratory ("new" USA Medical Research Institute of Infectious Diseases [USAMRIID]) could have implications for the Lawrence Livermore National Laboratory (LLNL) Biosafety Level-3 (BSL-3) facility, so we pro-actively assessed the situation. No problems were found. Details are given below.

In developing the LLNL BSL-3 Environmental Assessment (EA), one of the accident scenarios (maximum credible event [MCE]) cited was used in the "new" USAMRIID Environmental Impact Statement EIS. This accident scenario was considered not reasonably foreseeable by the NRC because the mathematical model used to calculate the possible aerosol release was proprietary and therefore not available to the NRC to make an independent determination. An attempt by the NRC to reproduce the findings in a different model did not produce the same result.

In view of the NRC's concern, it was decided to re-examine the consequences of the LLNL BSL-3 bounding accident using a publicly accessible dispersion model. The findings are contained in the report attached, "Bounding Accident Analysis for LLNL BSL-3 Facility". The report concluded that "the consequence estimates in the EA can be reproduced using a public-accessible Gaussian plume-dispersion model and conservative modeling assumptions consistent with the accident scenario postulated in the EA. Also, the potential consequences to the public for the postulated accident would be far below the minimum infectious dose of one organism."

Additionally, I have reviewed the recommendations made in the National NRC report, "*Evaluation of the Health and Safety Risks of the New USAMRIID High Containment Facilities at Fort Detrick, Maryland*", Committee of Review the Health and Safety Risks of High Biocontainment Laboratories at Fort Detrick, Board on Life Science Division on Earth and Life Studies (pre-publication, 2010) on the "new" USAMRIID EIS. I have commented on how these recommendations have been addressed by LLNL below.

1. **NRC Recommendation**: *USAMRIID should continue to set high standards for advancing security, operational, and biosurety measures.*

   LLNL: Maintains high standards for security, operational, and biosurety measures. Policies and practices in these areas are reviewed, audited and updated regularly. LLNL policies and procedures and the Select Agent Center Standard Operating Procedures (SOP) are reviewed and updated as needed, but at least annually.

2. **NRC Recommendation**: *Although USAMRIID has sought to set high standards for biosurety and biosafety, recent examples of laboratory-acquired infections (glanders and tularemia) and breaches in containment (B. anthracis spores) point to human error or deliberate misuse. The committee recommends further formalized training in responsibility and accountability at USAMRIID, similar to that required for NIH-sponsored training programs. The circumstances surrounding the laboratory-acquired infections also should be carefully evaluated to determine what lessons can be learned for preventing future cases.*

   LLNL: LLNL has the "*LLNL Standards of Conduct and Business Ethics*" booklet that sets out LLNL policy and expectations. In addition, a new on-line ethics training course (PS7023-W), entitled "*LLNS Business Ethics and Compliance*" is required training for all employees. There is no required training at this time for BSL-3 staff on the National Institutes of Health (NIH) training program mentioned above (*On Being A Scientist: Responsible Conduct in Research*, National Academy of Sciences, 1995 3rd ed.).

3. **NRC Recommendation**: *Given the unique nature of USAMRIID's mission in dealing with special pathogens, additional measures should be taken to provide assurance that experienced medical professionals are readily available to consult on unusual infectious diseases. Serious consideration should be given to support an initiative that would provide experienced specialist physicians knowledgeable of diseases caused by organisms studied at the laboratories. This would include consultation as needed on a 24/7 schedule to see patients from the community. Such physicians should also serve to provide continuing communication and coordination between USAMRIID scientists and community physicians and public health personnel.*

   LLNL: A LLNL physician from Health Services who is knowledgeable of the diseases being researched is available for personnel working in the BSL-3. This physician consults with laboratory personnel and the personal physicians of Select

Agent staff as needed. This physician has developed and conducts a training course in signs/symptoms, risks, prophylactics and treatment, and general backgrounds of diseases for the LLNL staff.

4. **NRC Recommendation**: *For medical emergency response mechanisms, a senior authoritative management system is needed to ensure that USAMRIID works effectively with country government agencies, the local medical community, emergency preparedness and response initiatives, and Frederick Memorial Hospital. Such a system would include a clear chain of command with designated personnel to work directly with partners in the county and community. The Army should consider the use of permanent civilian staff for these positions to ensure continuity of relationships. Because USAMRIID will be part of the National Interagency Biodefense Campus, which will include biocontainment facilities of two other agencies, consideration should be given to delineating and coordinating emergency and medical response plans and resources for all facilities on the campus.*

   LLNL: BSL-3 has a Select Agent Incident Plan (SAIRP) that is reviewed and drilled annually to ensure the plan's effectiveness. LLNL has an Emergency Response Organization (ERO) that can be activated if an incident occurs anywhere on the LLNL site. The ERO works with the surrounding communities' emergency response groups and hospitals in particular for medical emergencies.

5. **NRC Recommendation**: *USAMRIID should expand it two-way communications with the public. Examples of possible communication efforts are*
   a. *Promptly disclosing laboratory incidents to the public,*
      LLNL: Via the occurrence reporting process LLNL is diligent in disclosing all applicable lab events.
   b. *Providing fact sheets about pathogens being studied, to include information on their natural reservoirs and how they are transmitted, and*
      LLNL: General information about possible microorganims to be used was provided in the LLNL BSL-3 EA.
   c. *Holding an open house prior to the activation of the new USAMRIID facility or opening a visitors' center.*
      LLNL: The BSL-3facility is already operational.

6. **NRC Recommendation**: *USAMRIID should consider strategies that have been used by other containment laboratories to enhance community understanding and facilitate integration into the community. If possible, such communication*

strategies could be coordinated with the two other laboratories of the National Interagency Biodefense Campus.

LLNL: There are a number of communication means (LLNL Public Affairs Office, NEWSLINE, LLNL Science Education Program, etc), but none specific to the BSL-3. The most direct involvement is participation of non-affiliated community members on the Institutional Biosafety Committee (IBC) and the Institutional Care and Use Committee (IACUC). All research conducted in the BSL-3 is reviewed by one or both of these committees.

7. **NRC Recommendation**: *USAMRIID should involve the Frederick community in ongoing activities related to improving safety at the laboratory. For example, it might be useful to include community members on the Institutional Biosafety Committee (which reviews research involving Biohazardous risks) or other relevant committees.*

   LLNL: LLNL has community members on each of the following committees: the IBC, the IACUC, and the Institutional Review Board (IRB). These committees provide regulatory over-site and approval for all of the biological, animal and human subject research conducted at LLNL.

8. **NRC Recommendation**: *USAMRIID should create a community advisory board, with a broad representation of community views. This board should meet regularly to learn about successes, problems, and improvements in policies and practices; encourage public suggestions for improvements; and help shape the laboratory's public communications and activities—including the development of guidelines for reporting incidents to the public.*

   LLNL: The community involvement with the IBC, IRB and IACUC covers this in a specific rather than a general way for LLNL.

Should you have any questions or need additional information regarding this report, please contact Dr. Anderson at: anderson250@llnl.gov or (925) 423-4285.

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Attachment: "Bounding Accident Analysis for LLNL BSL-3 Facility." Dated 8/2010

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Bounding Accident Analysis for LLNL BSL-3 Facility[i]

Introduction

In the bounding accident analysis for the Environmental Assessment (EA) for the LLNL Biosafety Level 3 (BSL-3) Facility (Ref. 1), the accident scenario used was essentially the same as that used by the Department of the Army in its Final Programmatic Environmental Impact Statement (PEIS) for the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) at Ft. Detrick, Maryland (Ref. 2).

In a recent review of the PEIS by the National Research Council (NRC), (Ref. 3), the accident analysis was criticized because the mathematical model used to calculate the potential biological release was proprietary and therefore not available to the NRC to make an independent determination. An attempt by the NRC to reproduce the findings using a different model did not produce the same result.

In view of the NRC criticism, it was decided to re-examine the consequences of the LLNL BSL-3 bounding accident using a publicly accessible dispersion model. This current evaluation uses the Hotspot Health Physics Code (Ref. 4), a Department of Energy (DOE)-developed, publicly accessible Gaussian plume-dispersion model. Hotspot was developed by DOE as a tool for performing radiological event atmospheric dispersion consequence analysis. It is a companion dispersion model for the National Atmospheric Release Advisory Center (NARAC), which provides tools and services to the Federal Government that map the probable spread of hazardous material accidentally or intentionally released into the atmosphere. Hotspot is included as part of the DOE Safety Analysis Tool Chest for performance of Nuclear Safety Analysis calculations.

LLNL BSL-3 Accident Scenario

The accident scenario, as described in the EA, involves a release of a rickettsial microorganism, *Coxiella burnetii* (*C. burnetii*), which causes Q fever. A worker places one liter of *C. burnetii* slurry into six 250-ml polypropylene centrifuge tubes (165 milliliters per tube). The worker fails to insert the O-rings or tighten the screw-on centrifuge caps. The centrifuge, which is not in a biosafety cabinet, is turned on. All six tubes leak - with some of the slurry leaking into the rotor and some of it leaking into the centrifuge compartment.

It would not be credible to attribute more than 1% to 10% of the slurry leaking past an improperly sealed centrifuge tube. It is assumed 10% of the slurry (100 ml) leaks from the tubes.

It is likely that substantially more slurry leaking past improperly sealed caps would vent out and into the centrifuge cabinet than into the covered rotor. From this it may credibly be assumed that 1% of the slurry leaking from the tubes (1 ml) leaks onto the rotor – with the remaining slurry (99 ml) leaking into the centrifuge cabinet.

The scenario postulates that most (99%) of the slurry that leaked into the covered rotor is not aerosolized. Then the amount aerosolized would be 1% of 1 ml = 0.01 ml.

The scenario also postulates that only a fraction of the slurry that leaked into the centrifuge cabinet is aerosolized and 90% of that settles as droplets inside the chamber. It is credible to assume that, as with the covered rotor, 1 % of the slurry leaking into the centrifuge cabinet becomes aerosolized: 1% of 99 ml = 0.99 ml. Of this, 90% settles out as droplets inside the chamber and the remaining 10% is released as an aerosol: 10% of 0.99 ml = 0.099 ml.

Then the total quantity of aerosolized slurry released to the room upon opening the centrifuge lid would be 0.01 + 0.099 = 0.109 ml, approximately 0.11 ml.

The slurry is postulated to be thixotropic (much like egg white), with about 20% dry solids. Serum-albumin (crystalline) has a documented concentration by weight of 22%, with a solution density of 1.065 g/cc (Ref. 5). This appears consistent with the slurry description. Applying the serum-albumin solution density, the mass of the aerosolized slurry solids would be: 20% x 0.11 ml x 1.065 g/cc = 0.023 g.

Conservatively applying, in this case, the upper estimate for the number of *B. anthracis* spores per gram estimated in the 2001 terrorist attack involving letters sent to the Senate, 2 g of dry material could contain up to 1E12 organisms (Ref. 6), or 5E11 organisms per gram. Then the number of aerosolized *C. burnetii* organisms released to the room would be: 2.3E-2 x 5E11 = 1.2E10 organisms.

The estimated human infective dose (HID) with a 25 to 50 percent chance of contracting the disease through the inhalation route for Q fever is 10 organisms (Ref. 7). Then the number of HID_{50} aerosolized would be 1.2E10 organisms x 1 HID_{50} / 10 organisms = 1.2E9 HID_{50} aerosolized.

As stated in the accident scenario, the percent aerosol recovery (the percent of infectious doses of *C. burnetii* rendered airborne in a one- to five-micron particle size) representing the maximum infectivity for man is determined conservatively to be 0.1 percent. Thus the number of infectious aerosolized doses would be 0.1% x 1.2E9 HID_{50} = 1.2E6 HID_{50}.

<u>Source Term for the Dispersion Analysis</u>

The Source Term (ST) is the amount of material (in this case *C. burnetii* in terms of HID_{50}) released to the air. The airborne source term is typically estimated by the following five-component linear equation (Ref. 8):

ST = MAR x DR x AF x RF x LPF

where:

ST = Source Term
MAR = Material-at-Risk

DR	= Damage Ratio
AF	= Airborne Fraction
RF	= Respirable Fraction
LPF	= Leak Path Factor

The maximum number of aerosolized infectious doses of *C. burnetii* presented to the exhaust filters is: MAR x DR x AF = 1.2E6 HID_{50}

The air in the BSL-3 laboratory room in which the postulated accident takes place exhausts via two filters in series which are conservatively estimated to have 95% particulate removal efficiency, and then exits through a roof stack. Thus all but 5% of the material is captured by the filters and the LPF = 0.05. The lung retention of respirable particles is determined to be one half or less of the intake: RF $\leq$ 0.5.

Then the Source Term is:

ST = 0.05 x 0.5 x 1.2E6 HID_{50} = 3E4 HID_{50} *C. burnetii.*

<u>Dispersion Analysis</u>

Scenario Assumptions and Input

- Daytime event
- Release height = 0.0 m
- Pasquill stability class D, open (rural) terrain
- Mixing layer height = 100 m
- Wind speed = 4.5 mph (2.1 m/s) - as measured at 3 m
- Deposition velocity = 0.1 cm/s
- Organism die-off rate = ~1%/minute ($t_{1/2}$ = 70 minutes)
- Release Duration = Exposure Duration = Sample Time = 1.2 minutes
- Receptors of interest = 100 m and 810 m downwind from the exhaust stack.
- Receptor height = 0.0 m
- Maximally exposed individual breathing rate = 15 L/min (2.5E-4 m^3/s).

<u>Dispersion Analysis Results</u>

The dispersion analysis results in Table 1 provide an estimate for potential exposure to the public for the postulated accident scenario.

Table 1 : Dispersion Analysis Results

DISTANCE [Km]	χ/Q NORMALIZED ATMOSPHERIC DISPERSION COEFFICIENT [sec/m3]	χ RESPIRABLE TIME-INTEGRATED AIR CONCENTRATION [HID_{50}-sec/m3]	RESPIRABLE AIR CONCENTRATION [HID_{50}/L]	RESPIRABLE DOSE [HID_{50}]
0.016	2.10E-01	6.3E+03	8.4E-02	1.6E+00
0.038	3.80E-02	1.1E+03	1.5E-02	2.8E-01
0.100	5.60E-03	1.7E+02	2.2E-03	4.2E-02
0.810	1.10E-04	3.4E+00	4.5E-05	8.4E-04

Estimated Potential Dose Concentration to the Public:

- The dose concentration calculated at 16 m of 0.084 HID_{50}/L is consistent with the dose concentration result at 16 m of <0.1 HID_{50}/L presented in the EA.
- The dose concentration calculated at 38 m of 0.015 HID_{50}/L is consistent with the dose concentration result at 38 m of <0.01 HID_{50}/L presented in the /EA.
- It is further shown that the dose concentrations applicable to the nearest public receptor to the LLNL BSL-3 Facility would be 4.5E-05 HID_{50}/L.

Estimated Potential Dose to the Public:

- For the postulated accident, there would be sufficient respirable *C. burnetii* at 16 meters from the exhaust stack to represent slightly greater than one airborne human infective dose at a 50 percent rate for contracting the disease. It is predicted that beyond 20 meters human receptors would receive less than one HID_{50}.
- As previously noted, per the CDC, the HID_{50} for *C. burnetii* is 10 organisms. If the minimum infective dose (MID) is represented by a single organism, then it is predicted that human receptors at 100 m and beyond would receive well below the MID for the postulated accident scenario.

<u>Conclusion</u>

The conclusion of this evaluation is that the consequence estimates in the EA can be reproduced using a public-accessible Gaussian plume-dispersion model and conservative modeling assumptions consistent with the accident scenario postulated in the EA. Also, the potential consequences to the public for the postulated accident would be far below the minimum infectious dose of one organism.

References:

1. Lawrence Livermore National Laboratory, DOE/EA-1442R, *Final Revised Environmental Assessment for the Proposed Construction and Operation of a Biosafety Level 3 Facility at Lawrence Livermore National Laboratory, Livermore, CA* (January 2008)
2. Department of the Army, U. S. Army Medical Research and Development Command (USAMRDC), *Final Programmatic Environmental Impact Statement; Biological Defense Research Program*," Fort Detrick, Frederick, MD (April 1989)
3. National Research Council of the National Academies , *Evaluation of the Health and Safety Risks of the New USAMRIID High Containment Facilities at Fort Detrick, Maryland*, Committee to Review the Health and Safety Risks of High Biocontainment Laboratories at Fort Detrick, Board on Life Sciences Division on Earth and Life Studies (pre-publication, 2010)
4. Lawrence Livermore National Laboratory, *Hotspot - Health Physics Codes, Version 2.07*, Steve Homman (March 2009)
5. Lister Institute, *The Density and Solution Volume of Some Proteins*, Harriette Chick, Charles James Martin, (November 1912)
6. U.S. Department of Homeland Security, *National Bio and Agro-Defense Facility, Final Environmental Impact Statement, Appendix E, Accidents Methodology*, (December 2008)
7. Centers for Disease Control and Prevention, *Biosafety in Microbiological and Biomedical Laboratories*, U.S. Department of Health and Human Services, Public Health Service, CDC and National Institutes of Health (NIH), Fourth Edition, Washington, DC (April 1999)
8. Department of Energy, DOE-HDBK-94, *DOE Handbook, Airborne Release Fractions/Rates and Respirable Fractions for Nonreactor Nuclear facilities, Volume I – Analysis of Experimental Data* (December 1994)

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[i] Calculations is this report were performed by Safety Analyst Mark Johnson, LLNL Safety Basis Division (August 2010)